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10/524,019	02/09/2005	Masahiko Tanikawa	TANIKAWA1	7565

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EXAMINER	
UNDERDAHL, THANE E	

ART UNIT	PAPER NUMBER
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/524,019	TANIKAWA ET AL.	
	Examiner	Art Unit	
	THANE UNDERDAHL	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9/24/09*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6,8,11,12 and 19-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6,8,11,12 and 19-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/2/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

This Office Action is in response to the Applicant's reply received 9/24/09. Claims 1, 3-6, 8, 11, 12, 19-27 are pending. No Claims are withdrawn. Claims 2, 7, 9-10, and 13-18 are cancelled. Claims 1 and 20 have been amended. Claims 25-27 are new. Claims 1, 3-6, 8, 11, 12, 19-27 are considered in this Office Action.

Response to Applicant's Arguments

In the response submitted by the Applicant the following 35 U.S.C § 103 (a) rejections are withdrawn:

- Claims 1, 3, 4, 11, 12, 19-21 and 24 as being obvious over Bohr et al. (U.S. Patent # 6060293) in light of support from 3 entries of Wikipedia (Electric Field, Dielectric Heating, Magnetic Field)
- Claims 1, 3-6, 11, 12, 19-24 as being unpatentable over Bohr et al in further view of Plantanias et al. (JCO, 1991) and further support from Rosse et al. (ASH, Hematology 2000).
- Claims 1, 3-6, 8, 11, 12, 19-24 as being unpatentable over Bohr et al. in further view of Cohen et al. (U.S. Patent # 3308809).

The Applicant's amendments limiting the magnetic field as a magnetostatic field necessitated the above withdrawal since Bohr et al. deals with AC magnetic fields.

New Rejections Necessitated by Amendment

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, 4, 11, 12, 19-21, and 24-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mehta et al. (Biotechnology Techniques, 1997) in light of support by Goldfarb et al. (Units for Magnetic Properties, 1985) and mindat.org (Magnetite Mineral Information).

These claims are drawn to a method of stabilizing a recombinant protein solution formulation or recombinant protein-containing solution by storing these solutions under a magnetostatic field with a magnetic flux density of 1mT or more. The recombinant protein is a physiologically active protein that is isolated and purified selected from the group such as an antibody, enzyme, cytokine and hormone. Dependant claims limit the protein composition is in a pharmaceutically acceptable carrier such as water.

Claim 12 includes the limitation that "wherein the recombinant protein-containing solution is a bulk solution for protein production". M.P.E.P. § 2111.04 states:

> Claim scope is not limited by claim language that suggests or makes optional but does not require steps to be performed, or by claim language that does not limit a claim to a particular structure

Claim 12 does not include a step that proteins are produce in the solution. Also claim 12 does not limit that the recombinant protein mentioned in claim 1 is produce in this solution. Therefore any art reading on any solutions that can support protein production of any form reads on these limitations. This includes any buffers that can be contaminated with bacteria or yeast or other microorganism that inherently produce proteins. This claim also reads on a reaction solutions that modify since the modified proteins are "produced" in the solution.

Mehta et al. teaches three proteins including isolated and purified bovine serum albumin, bovine alkaline phosphotase (pg 494, col 1), and dispase (pg 496, col 1) were immobilized on magnetic beads made of magnetite (pg 493, col 2) to produce proteins linked to magnetic beads in a bulk solution (Abstract). Mehta et al. teach that both bovine alkaline phosphotase and dispase remained physiologically active enzymes (pg 496, col 1). Mehta et al. teach that the alkaline phosphatase was immobilized to the magnetite and stored in protein solution formulation of BSA and phosphate buffer that inherently comprises water (pg 494, col 1).

Mehta et al. teaches that their magnetite particles have a magnetic polarization of 83.3 emu/g (Table 1). This inherently converts to a magnetic flux density of 54.2 mT as detailed in Formula A. Alternatively even when coated with a protein the magnetic beads have a magnetic polarization of 63.3 emu/g which converts to 41.4 mT and thus meets the limitations of greater than 1 mT. Therefore the proteins immobilized on the magnetite beads are exposed to a magnetostatic field greater than 1 mT. Mehta et al. teaches the active step of "storing the protein solution formulation under a magnetostatic field" and they also inherently teach "storing" the enzymes since these solutions with the magnetic beads are contained in some form for their respective activity assays. Therefore since the applicant does not provide any limitation on how long the enzymes are "stored" the broadest reasonable interpretation reads on any amount of time the protein solution formulation is contained.

Formula A: Magnetite inherently has magnetic flux density (MFD) greater than 1mT

Convert magnetization to magnetic polarization of magnetite (from Table 1 of Mehta and mindat.org)

$$\frac{83.3emu}{1gMagnetite}\times\frac{5.18gMagnetite}{1cm^3}=431.5emu/cm^3$$

Conversion factor for magnetic flux density to magnetic polarization (from Goldfarb et al.)

$$1T=\frac{10^4}{4\pi}emu/cm^3$$

Use above conversion factor to change magnetic polarization to magnetic flux density of magnetite

$$431.5emu/cm^3\times\left(\frac{4\pi}{10^4}\bullet\frac{T}{emu/cm^3}\right)=54.2mT$$

While Mehta et al. does not teach if all three isolated and purified enzymes are native or recombinant, this would be obvious to one of ordinary skill in the art since recombinant enzymes are art recognized equivalents for the same purpose as their native counterparts so it would be obvious to substitute one for the other since they have the same peptide sequence and perform the same reaction (M.P.E.P. § 2144.06 II).

Therefore claims 1, 3, 4, 11, 12, 19-21, and 24-27 are obvious in view of the above references.

Claims 1, 3, 4, 8, 11, 12, 19-21, 24-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cerdan et al. (Magnetic Resonance in Medicine, 1989).

The descriptions of claims 1, 3, 4, 11, 12, 19-21, and 24-27 are recited in the 35 U.S.C § 103 rejection above over Mehta et al. Claim 8 limits that the formulation is in a pre-filled syringe.

Cerdan et al. teach magnetite beads coated with isolated and purified monoclonal antibodies (Abstract). As mentioned in the 103 rejection over Mehta et al., magnetite inherently has a magnetostatic field greater than 1 mT. Therefore these monoclonal antibodies are exposed to a field greater than 1 mT. Cerdan et al. teach that the immobilized monoclonal antibodies are produced in a HEPES buffer solution by binding them to magnetite particles (pg 152, 2nd half). This magnetite/antibody is stored in HEPES buffer before used in various assays (pg 152, 2nd half) such as cell binding assays in PBS/BSA buffer, in vivo experiments (pg 153, top). Aqueous HEPES buffer was also used to store the magnetite beads bound to the antibodies before, after and during NMR experiments (pg 154). Cerdan et al. teach that this solution of magnetite and antibodies can be formulated into a syringe for injection during in vivo experiments (pg 153).

While Cerdan et al. does not teach these isolated and purified antibodies are native or recombinant, this would be obvious to one of ordinary skill in the art since recombinant antibodies are art recognized equivalents for the same purpose as their native counterparts so it would be obvious to substitute one for the other since they

have the same peptide sequence and have the same binding affinity (M.P.E.P. § 2144.06 II).

Therefore claims 1, 3, 4, 8, 11, 12, 19-21, 24-27 are obvious in view of the above references.

Claims 1, 3, 4, 5, 6, 8, 11, 12, 19-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cerdan et al. as applied to claims 1, 3, 4, 8, 11, 12, 19-21, 24-27 above, and further in view of Skibeli et al. (Blood, 2001).

The descriptions of claims 1, 3, 4, 8, 11, 12, 19-21, 24-27 are recited in the 35 U.S.C § 103 rejection above and are applied here as well. Claims 5, 6, 22 and 23 limit that the recombinant protein is a hematopoietic factor such as **erythropoietin** (**EPO**).

While Certan et al. teaches magnetic particles that are bound to antibodies they do not teach EPO. Regardless this would be obvious to one of ordinary skill in the art by the time the invention was made in view of the teachings of Skibeli et al.

They teach that EPO can be isolated with magnetic beads that are coated with anti-hEPO antibodies (Skibeli, pg 3628, col 1, 2nd half and Figure 1). Therefore Skibeli et al. teach that EPO is bound to the magnetic beads that will inherently have a magnetostatic field. However Skibeli et al. is silent as to the strength of that field.

However since Cerdan et al. already teach a method of binding antibodies to magnetite, it would be obvious to modify them to bind anti-hEPO antibodies. Therefore it would be obvious to one of ordinary skill in the art to substitute these anti-hEPO-magnetite particles to capture and store EPO in the method of Skibeli et al. since this is

a simple substation of one magnetic particle known to bind antibodies for another ((KSR Int'l Co. v. Teleflex, Inc. 550 U.S. 398 (2007) pg 14). Therefore the magnetite particles that are bound with anti-hEPO that has captured EPO will inherently expose and store the EPO in a field greater than 1mT since that is the measured magnetic flux density of magnetite.

Therefore claims 1, 3, 4, 5, 6, 8, 11, 12, 19-27 are obvious in view of the above references.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

In response to this office action the applicant should specifically point out the support for any amendments made to the disclosure, including the claims

(MPEP 714.02 and 2163.06). Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending U.S. applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to this Office action.

CONTACT INFORMATION

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thane Underdahl whose telephone number is (571) 272-9042. The examiner can normally be reached Monday through Thursday, 8:00 to 17:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Thane Underdahl
Art Unit 1651

/Leon B Lankford/
Primary Examiner, Art Unit 1651